

## Identification of an immunodominant *Babesia gibsoni* 47-kDa antigen

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### Abstract

The inosine monophosphate dehydrogenase (IMPDH) enzyme has been characterized and validated as a molecular drug target in other apicomplexans but not in the genus *Babesia*. Subsequently, we cloned and expressed a *Babesia gibsoni* IMPDH (BgIMPDH) cDNA in *Escherichia coli*. We also determined the inhibitory effect of mycophenolic acid (MPA) on recombinant BgIMPDH (rBgIMPDH) activity and the *Babesia* growths in vitro. The translated BgIMPDH peptide contained thirteen amino acid residues responsible for substrate and cofactor binding in its catalytic domain with Gly374 in BgIMPDH being replaced by Ser388 in mammalian IMPDH. The native BgIMPDH enzyme in the parasite was approximately 54-kDa mass similar to His-tagged BgIMPDH protein. The  $K_m$  values of the BgIMPDH were  $8.18 \pm 0.878$  (mean  $\pm$  standard error of the mean)  $\mu\text{M}$  and  $360.80 \pm 43.41$   $\mu\text{M}$  for IMP and  $\text{NAD}^+$ , respectively. MPA inhibited the rBgIMPDH activity yielding a  $K_i$  value of  $20.93 \pm 1.83$   $\mu\text{M}$  with respect to  $\text{NAD}^+$ . For *Babesia* growths, the  $\text{IC}_{50}$ s were  $0.95 \pm 0.21$  and  $2.88 \pm 0.49$   $\mu\text{M}$  for *B. gibsoni* and *B. bovis*, respectively. Therefore, our results suggest that MPA may inhibit the proliferation of *Babesia* parasites by targeting IMPDH enzyme of the purine pathway.